

REMARKS

Claims 21, 28, 29, 34-38, and 40 are under examination in this case. These claims stand rejected under 35 U.S.C. § 112, second paragraph, and 35 U.S.C. § 102. These rejections are addressed below.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 21, 28, 29 and 34-38 stand rejected under 35 U.S.C. § 112, second paragraph on the basis that substituted R_5 may be $(CH_2)_g(CH_3)_h$ in which $g + h = 0$, and that this would result in an incomplete structure. This option has been deleted from independent claim 21, and the indefiniteness rejection may be withdrawn.

Rejections under 35 U.S.C. § 102

Claims 21 and 34-38 stand rejected under 35 U.S.C. § 102(b) over Stürzebecher (DE 10029014 A1). This rejection is based on the assertion that, in paragraph [0025], Stürzebecher discloses the hydrochloric acid salt of benzenesulfonyl-D-Ser-Gly-4-amidino-benzylamide and that this compound corresponds to a compound of claim 21 in which R_4 is C_1 alkyl. This rejection is respectfully traversed.

As an initial matter, Applicants point out that, in all likelihood, the positive charge of the hydrochloric acid salt of benzenesulfonyl-D-Ser-Gly-4-amidino-benzylamide is located at the amidino group. Two of the other three remaining nitrogen atoms of the compound of Stürzebecher are part of amide bonds, and as such they are involved in the amide-resonance which leads to a decrease of their basicity. The only other remaining nitrogen atom is in close proximity to the partially positively charged sulfur of the sulfonyl group and therefore its basicity is also diminished. Accordingly, the positive charge will presumably be present only at the amidinium cation resulting from the protonation of the amidino group. This group is able to delocalize the positive charge resulting from the protonation and features a higher electron density that makes its

nitrogen atoms more basic than the other nitrogen atoms within this molecule. Moreover, the amidino group contains two nitrogen atoms so that the possibility for the proton to be bonded at this group is much higher than at the other nitrogen atoms of this molecule.

According to claim 21 as presently on file, the compound of general formula I is “characterized in that one or more charged radicals, derived from -COOH , -CH(COOH)_2 , $\text{-SO}_2\text{H}$, -NH_2 , an amidino, hydroxylamidino, amidrazono, or guanidine group, are present in the radicals R_1 , R_2 , R_3 or R_5 .” Considering the respective definition for the compound of Stürzebecher, there is no corresponding radical R_1 , the radicals R_2 and R_3 are both hydrogen atoms, R_4 is a hydroxyl methylene group, and R_5 is a benzyl group. However, none of these radicals has a basic functionality. Taking into account that the hydrochloric acid salt of Stürzebecher is an equimolar composition, in all likelihood the proton will be bonded at the amidino group which is also the most basic functional group of this molecule. However, in claim 21, the presence of a positive charge in the amidino group of the benzyl is not claimed. Accordingly, the compound of Stürzebecher cannot anticipate the compounds according to claim 21 of the present invention. The same is true for dependent claims 34-38. This basis for the rejection may be withdrawn.

Claims 21, 34, 35, 37, and 38 also stand rejected under 35 U.S.C. § 102(b) as being anticipated by Tamura et al. (Bioorganic and Medicinal Chemistry Letters, 2000, 10: pages 983-987). This rejection is based on the assertion that the trifluoroacetic acid salt of compound 1a (U is a heterocyclohexyl radical, R_5 is COOR_{12} , R_{12} is a branched C_4 alkyl, and in $V_n = 0$) falls under the definition of the compounds covered by claim 21. Applicants respectfully disagree.

The heterocyclohexyl radical of compound 1a of Tamura also has a hydroxyl substitution in position 2. However, such substituted heterocyclohexyls are not claimed in claim 21. According to claim 21, U of general formula I “is a phenyl or cyclohexyl radical or a heterophenyl or heterocyclohexyl radical having at least one N , S , or O as

heteroatom.” From the wording of claim 21, one skilled in the art would understand that the heteroatoms can only be part of these rings. If the heteroatoms could also refer to *substituents* of the ring, a definition for at least one further radical for the heteroatoms would be mandatory. Otherwise, the heteroatoms N, S, and O would have only one binding partner which, in particular for a phenyl or heterophenyl radical, would not make any sense. Quite to the contrary, the definition of U in claim 21 does not provide for these further radicals. Accordingly, the heteroatoms clearly and ambiguously refer only to the heteroatoms that are part of the listed rings. And, consequently, compound 1a is not encompassed by and therefore cannot anticipate the present claims.

Further, as shown in scheme 3, the positive charge resulting from the trifluor acetic acid is located at the amidinium group resulting from the protonation. According to claim 21, the positively charged radicals can only be present at R₁, R₂, R₃, and R₅. In the case of Tamura compound 1a, there is no radical R₁, R₂ is a methyl group, R₃ is a hydrogen atom, R₄ is a hydroxyl methylene group, and R₅ is a 2-methyl propyl ester group. However, it has to be considered that the N-amidino pyridinyl group represents a derivative of guanidine. Due to the resonance stabilizing effect of the three nitrogen atoms in the guanidinium cation, guanidine is one of strongest organic bases, and as such, comparable with alkali hydroxide with respect to its strength ($pK_B = 0.35$). Undoubtedly, the positive charge is present in this part of the molecule. However, taking into account the definition of the charged radicals according to claim 21, neither an amidino nor a guanidine group at that position of the Tamura molecule can have a positive charge. Therefore, compound 1a of Tamura does not fall within independent claim 21 and cannot anticipate this claim or dependent claims 34, 35, 37, or 38. This rejection may also be withdrawn.

CONCLUSION

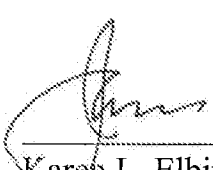
Enclosed is a Petition to extend the period for replying to the Office action for one month, to and including November 17, 2008. Please apply a \$65.00 extension fee to Deposit Account No. 03-2095.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

James DeCamp
Reg. No. 43,580

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Karen L. Elbing, Ph.D.
Reg. No. 35,238

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045